(12) A. R. Katritsky and J. M. Lagowski, "Chemistry of the Heterocyclic N-Oxides", Academic Press, New York, N.Y., 1971, p 153 ff.
(13) E. C. Taylor and P. A. Jacobi, *J. Am. Chem. Soc.*, **95**, 4455 (1973).
(14) S. Sternhell, *Q. Rev., Chem. Soc.*, **23**, 236 (1969).
(15) T. Cohen and G. L. Deets, *J. Org. Chem.*, **37**, 55 (1972).
(16) C. R. Noller and I. Bergsteinsson, "Organic Syntheses", Collect. Vol. II, Wiley, New York, N.Y., 1943, p 164.

A New Pathway for Oxidation of Alcohols to Carbonyl Compounds[1]

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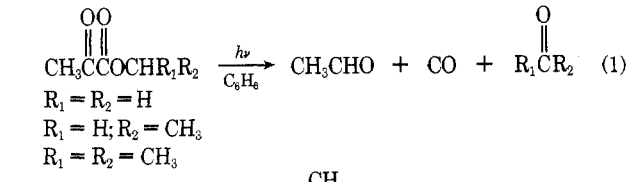
In the early 1960's several research groups studied the photochemistry of alkyl esters of pyruvic acid. Arising from these studies were the findings that in benzene pyruvates fragment photochemically as shown in eq 1[2,3] but they pho-

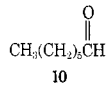
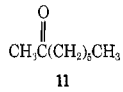
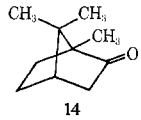
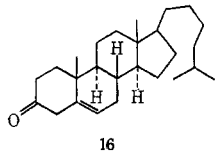
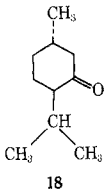
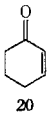


toreduce when hydrogen donating solvents are used[4] (eq 2). Any interest in utilizing pyruvate photoreaction as a synthetic tool was tempered by the knowledge that the available syntheses of these compounds employed unacceptably forcing conditions for use with sensitive materials.[5] A recent report[6] of a new, simple synthesis of the acid chloride of pyruvic acid raised the possibility that esters of this acid easily could be formed under mild conditions and that synthetically useful photochemical reactions involving these compounds now could be considered. Specifically, the synthesis of pyruvates followed by their reaction as shown in eq 1 could represent an effective sequence for oxidation of alcohols to carbonyl compounds. Assuming that this oxidation sequence could be of general value, a variety of pyruvates were synthesized and irradiated. The results from study of these reactions suggest that the pyruvate oxidation sequence could be useful in solving problems of synthesis in a variety of areas.

In the opening phase of this investigation, the pyruvate esters of seven alcohols [1-phenylethanol (1), benzyl alcohol (2), 1-heptanol (3), 2-octanol (4), cyclohexanol (5), cyclopentanol (6), and borneol (7)] were prepared and irradiated. Alcohol esterification was quantitative. Photochemical reaction of the resulting esters, although not usually quantitative, produced good to excellent yields of the carbonyl compounds 8–14 (Table I). Analysis of the information in Table I reveals the following features for the pyruvate oxidation sequence: (a) the oxidation sequence works well for simple compounds of various structures; (b) primary alcohols are oxidized to aldehydes without further reaction; and (c) essentially complete photochemical reaction of pyruvates can be accomplished without noticeable secondary reaction.

The effect of five solvents on the photochemical reaction of 1-phenylethyl pyruvate is summarized in Table II. The photochemical process is quite solvent dependent. Benzene is an excellent choice and carbon tetrachloride appears to be equally good. Pentane and ethyl ether are poor reaction solvents since irradiation in either of these two results in considerable solvent incorporation.[4]

Table I. Alcohol Oxidation Products and Yields

Alcohol	Oxidation product	Yield, %	Unreacted alcohol, %
1	 8	100	None
	 9	95	4
3	 10	77	6
4	 11	85	None
5	 12	100	None
6	 13	84	None
7	 14	85	1
15	 16	80	None
17	 18	88	None
19	 20	76	2

Since the pyruvate synthesis–photoreaction combination was effective for oxidation of alcohols which are relatively easily oxidized, it was decided to test this combination in several situations where the oxidation products are known to be capable of facile, further reaction or where other reactions could intervene. Conditions for oxidation of cholesterol (15), for example, easily lead to isomerization of the carbon–carbon double bond into conjugation with the newly formed carbonyl.[7,8] In order to determine whether the pyruvate oxidation pathway would also lead to this isomerization, the pyruvate ester of cholesterol was synthesized and irradiated. No isomerization was observed; a good yield (Table I) of the nonconjugated enone (16) was obtained.

Oxidation of alcohols to aldehydes and ketones can be complicated by epimerization at the center next to the carbonyl. Conversion of menthol (17) to menthone (18), for example, is accompanied by formation of isomenthone, unless precautions are taken.[9] To test the possibility of epimerization in the pyruvate oxidation sequence, methyl pyruvate was

Table II. Irradiation of 1-Phenylethyl Pyruvate in Various Solvents

Solvent	Acetophenone yield, %
Benzene	100
Carbon tetrachloride	95
Acetone	86
Pentane	31
Ethyl ether	17

synthesized, irradiated, and found to produce methone (**18**) (Table I) with no detectable isomenthone present.

Oxidation of allylic alcohols can result in attack by the oxidizing agent on the double bond.[10] To investigate whether the pyruvate oxidation sequence avoids this competing pathway, 2-cyclohexen-1-ol (**19**) was studied. Oxidation of **19** proceeded in the normal manner to give 2-cyclohexen-1-one in good yield (Table I).

Pyruvate oxidation was unsuccessful in oxidation of *trans*-cinnamyl alcohol to *trans*-cinnamaldehyde. Although esterification occurred in the normal manner, irradiation of *trans*-cinnamyl pyruvate (**21**) resulted in isomerization to the cis isomer. This is not a surprising result when one considers that esters of pyruvic acid are believed to react via an excited triplet state[2,3] and the triplet state energy of the styrene chromophore should be lower in energy [E_t (styrene) = 61.7 kcal/mol[11]] than that of the keto ester portion [E_t (methyl pyruvate) = 65 kcal/mol[2,12]] of the molecule. Excitation absorbed by the keto ester chromophore would be transferred to the double bond and produce isomerization.

It would be desirable to conduct the pyruvate oxidation process without isolating the intermediate pyruvate ester. This possibility was investigated by irradiating directly the reaction mixture from esterification of 1-phenylethanol (**1**). The yield of acetophenone arising from this abbreviated procedure was good (90%); however, the reaction mixture had become quite dark during irradiation, a result of decomposition of pyridinium hydrochloride.

It is possible to oxidize alcohols to aldehydes and ketones using the pyruvate oxidation sequence described here without allowing the temperature of the reaction mixture to rise above room temperature. Further, no acids or inorganic oxidizing agents ever come in contact with the starting materials or products. Pyridine, the strongest base used, is involved only in the esterfication step. These reaction conditions must be among the mildest available for alcohol to carbonyl oxidations.

Experimental Section

General Procedures. The esterification, irradiation, and isolation procedure used for oxidation of each of the alcohols **1–7, 17,** and **18** was identical. This procedure is described below.

A. Esterfication. The alcohol to be esterified (0.03 mol) and dry pyridine (0.033 mol) were dissolved in 100 ml of anhydrous benzene. Pyruvoyl chloride[6] (0.03 mol) in 50 ml of benzene was added in a dropwise manner with stirring. Precipitation of pyridinium hydrochloride was immediate. Cooling with cold water was necessary to keep the reaction mixture at 25 °C. After stirring for 15 min, the pyridinium hydrochloride was removed by filtration and the benzene distilled in vacuo to yield the pyruvate ester contaminated with pyridinium hydrochloride. The contaminant could be removed by dissolving the reaction mixture in 50 ml of carbon tetrachloride, allowing it to stand for a few hours, and filtering the insoluble material. When the carbon tetrachloride was evaporated from the filtrate, a quantitative yield of the appropriate ester remained.

The identity of each ester was established first by instrumental analysis [NMR (Varian T-60) and GC/MS (Finnigan 1015-D)] and then by saponification to the starting alcohol and sodium pyruvate. Stirring the ester for 12 h in a 1% solution of sodium hydroxide in methanol was sufficient for total saponification.

B. Irradiation and Isolation. The pyruvate ester (4.0 mmol) was dissolved in 350 ml of dry benzene and the solution purged with nitrogen for 1 h. The nitrogen purge was continued during Pyrex-filtered irradiation with a 450-W, medium-pressure Hanovia mercury lamp. After 1 h, the irradiation was stopped, the reaction mixture analyzed by GC/MS, the benzene removed by fractional distillation, and the residual liquid distilled in vacuo using a Buchi/Brinkmann microdistillation oven to give the products shown in Table I. Each product was compared by NMR and GC/MS with a known sample (Aldrich Chemical Co.). In several cases (Table I) small amounts of the starting alcohol were detected. For products **5, 6, 7,** and **19,** noticeable losses occurred during solvent removal; thus, the product yields as determined prior to solvent removal are given in Table I.

Oxidation of Cholesterol (15). Compound **15** was esterified and irradiated in the same manner as the other alcohols; however, the oxidation product **16** crystallized from the reaction mixture following benzene removal and was recrystallized from methanol rather than distilled. Compound **16** was identified by comparison with a known sample.[8]

Effect of Solvent on Pyruvate Oxidation. The effect of solvent change on the pyruvate oxidation process was tested by successively replacing benzene with carbon tetrachloride, acetone, ethyl ether, and pentane as an irradiation solvent in photolysis of 1-phenylethyl pyruvate. The results are shown in Table II. NMR spectra of crude reaction mixtures from irradiations in ethyl ether and pentane showed considerable solvent incorporation.

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Registry No.—**1,** 98-85-1; **2,** 100-51-6; **3,** 111-70-6; **4,** 123-96-6; **5,** 108-93-0; **6,** 96-41-3; **7,** 507-70-0; **8,** 98-86-2; **9,** 100-52-7; **10,** 111-71-7; **11,** 111-13-7; **12,** 108-94-1; **13,** 120-92-3; **14,** 76-22-2; **15,** 57-88-5; **16,** 601-54-7; **17,** 1490-04-6; **18,** 89-80-5; **19,** 822-67-3; **20,** 930-68-7; pyruvoyl chloride, 5704-66-5.

References and Notes

(1) A portion of this work has appeared in preliminary form: R. W. Binkley, *Synth. Commun.*, **6,** 281 (1976).
(2) G. S. Hammond, P. A. Leermakers, and N. J. Turro, *J. Am. Chem. Soc.*, **83,** 2395 (1961).
(3) (a) P. A. Leermakers, P. C. Warren, and G. F. Vesley, *J. Am. Chem. Soc.*, **86,** 1768 (1964); (b) P. A. Leermakers, M. E. Ross, G. F. Vesley, and P. C. Warren, *J. Org. Chem.*, **30,** 914 (1965).
(4) N. C. Yang and A. Morduchowitz, *J. Org. Chem.*, **29,** 1654 (1964).
(5) Reference 3a, p 1770.
(6) H. C. J. Ottenheijm and J. H. M. de Man, *Synthesis*, 163 (1975).
(7) (a) R. V. Oppenauer, "Organic Syntheses", Collect. Vol. III, E. C. Horning, Ed., Wiley, New York, N.Y., 1955, pp 207–209; (b) J. F. Eastham and R. Teranishi, "Organic Syntheses", Collect. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N.Y., 1963, pp 192–195; (c) L. F. Fieser, "Organic Syntheses", Collect. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N.Y., 1963, pp 198–199.
(8) An example of a procedure which does not lead to isomerization of the double bond is given by L. F. Fieser and K. L. Williamson in "Organic Experiments", D. C. Heath, Lexington, Mass., 1975, p 108.
(9) (a) H. C. Brown, C. P. Garg, and K.-T. Liu, *J. Org. Chem.*, **36,** 387 (1971); (b) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83,** 2952 (1961).
(10) E. Glotter, S. Greenfield, and D. Lavie, *J. Chem. Soc. C*, 1646 (1968).
(11) S. L. Murov, "Handbook of Photochemistry", Marcel Dekker, New York, N.Y., 1973, p 30.
(12) J. F. Arnett, D. B. Larson, and S. P. McGlynn, *J. Am. Chem. Soc.*, **95,** 7599 (1973).

Stereochemistry of Hydroboration–Oxidation of Terminal Alkenes[1]

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Hydroboration of alkenes followed by alkaline hydrogen peroxide oxidation of the resulting alkylboranes is the method of choice for the anti-Markownikoff hydration of carbon–carbon double bonds.[2] Although mechanistic studies have